IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/648536 Confirmation No. 4649
Applicant	:	LOCKERBIE, Robert Owen, et al.
Filed	:	08/25/2003
Title:		Induction of and Maintenance of Nucleic Acid Damage in Pathogens Using Riboflavin and Light
TC/A.U.	:	1656
Examiner	:	LEE, Jae W.
Docket No.	:	B0175-US02
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APPEAL BRIEF UNDER 37 C.F.R 41.37

Pursuant to 37 C.F.R 41.37, Appellants submit this Appeal Brief to the Board of Patent Appeals and Interferences, for Applicant's appeal from the July 30, 2010 Final Office Action. In light of the Notice of Appeal filed on October 5, 2010, this Appeal Brief is being timely filed along with payment of the Appeal Brief fee as set forth in 37 C.F.R. 41.37(a)(1) and (2).

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I. Real Party in Interest

The real party in interest is CaridianBCT Biotechnologies, LLC (formerly known as Navigant Biotechnologies, LLC, change of name recorded on July 28, 2008, Reel/Frame 021301/0079), the assignee of the entire right, title and interest in the application at issue.

II. Related Appeals and Interferences

There are currently no related appeals or interferences pending before the Board of Patent Appeals and Interferences.

III. Status of Claims

Claims 1-11, 16, 20-21, and 23 were cancelled. Claims 12-15, 17-19 and 22 stand rejected. Therefore, claims 12-15, 17-19 and 22 are the subject of this appeal.

The claims are set forth in the attached Appendix (pages 16-17).

IV. Status of Amendments

Claims 1-11, 16, 20-21, and 23 were cancelled and claims 12-15, 17-19 and 22 were amended by Applicants in the Amendment after Final filed on May 5, 2009. The Examiner entered the claim amendments in the Non-Final Office Action dated May 20, 2009. No further claim amendments have been filed by Applicants.

V. Summary of Claimed Subject Matter

Independent claim 15 is directed toward a process for inactivating white blood cells which may be contained in a fluid. The steps of this process include: adding to the fluid containing white blood cells an effective amount of riboflavin acting as a photosensitizer (page 8, lines 10-18 and 20-24); exposing the fluid and riboflavin acting as a photosensitizer to light of an appropriate wavelength which is within UVB range to activate the riboflavin acting as a photosensitizer and cause damage to the nucleic acid of the white blood cells (page 8, lines 29-31; Examples 1- 3); and substantially maintaining the damage to the nucleic acids of the white blood cells (page 8, lines 1-5; Example 1).

Dependent claim 12 is directed toward an optional component of the to-be-treated fluid which is red blood cells (page 9, Example 1).

Dependent claim 13 is directed toward an optional component of the to-be-treated fluid which is platelets (page 9, Example 1).

Dependent claim 14 is directed toward an optional component of the to-be-treated fluid which is plasma (page 9, Example 1).

Dependent claim 17 is directed toward a fluid suitable for transfusing into a patient comprising red blood cells treated by the process of claim 15 (page 8, lines 31-33).

Dependent claim 18 is directed toward a fluid suitable for transfusing into a patient comprising platelets treated by the process of claim 15 (page 8, lines 31-33).

Dependent claim 19 is directed toward a fluid suitable for transfusing into a patient comprising plasma treated by the process of claim 15 (page 8, lines 31-33).

Independent claim 22 is directed toward a process for providing pathogen-reduced blood or blood components. The steps of this process include: damaging the nucleic acid of any pathogenic white blood cells, bacteria or viruses which may be present with the blood or blood components (page 8, lines 1-7; lines 24-26; lines 29-33); adding riboflavin to the fluid containing blood or blood components (page 8, lines 20-24); and exposing the blood or blood components and riboflavin acting as a photosensitizer to UV or visible light to activate the riboflavin acting as a photosensitizer to fragment the nucleic acid of the pathogenic white blood cells, bacteria or viruses (page 8, lines 29-31; Example 3-5).

VI. Grounds of Rejection To Be Reviewed on Appeal

A. Whether the rejection of claims 12-15, 17-19 and 22 under 35 USC 103(a) as being unpatentable over Goodrich et al. (US Patent 6,258,577) in view of Joshi PC (Comparison of the DNA-damaging property of photosensitized riboflavin via single oxygen (1O2) and superoxide radical O2-, Mechanisms, Toxicol Lett. 1985,26(2-3):211-7) should be reversed.

VII. Argument

A. The rejection of claims 12-15, 17-19 and 22 under 35 USC 103(a) as being unpatentable over Goodrich et al. in view of Joshi PC should be reversed.

Applicants believe the Examiner has not made a prima facie case of obviousness over the combined teaching of the prior art.

As set forth in MPEP 2143, "The rational to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." *KSR International Co. v. Teleflex Inc.*

All of the elements of Applicants' claimed invention were not known from either the Goodrich or Joshi references alone or in combination.

There is no disclosure in Goodrich of using riboflavin and light (at any wavelength) to inactivate white blood cells. Column 4, line 5 of Goodrich lists the microorganisms that may be treated with riboflavin and light. Viruses, bacteria, fungi and protozoa are listed. White blood cells are not. Consequently, there is also no disclosure of using riboflavin and light to cause damage to the nucleic acids of white blood cells and substantially maintaining the damage to the nucleic acids of white blood cells as Applicants' claim. Thirdly, and as the Examiner admits, Goodrich does not disclose the specific use of UVB light to inactivate white blood cells.

The Examiner argues on page 5 of the final office action that "Goodrich et al teach irradiating UV light to "whole blood" or "blood constituents" or "separated blood products", "bacteria" and/or "viruses" which one of skill in the art would interpret to be inclusive of red blood cells, white blood cells, platelets, plasma, bacteria and/or viruses in the presence of riboflavin acting as a photosensitizer..."

Therefore, the Examiner argues, one skilled in the art would figure out how to inactivate white blood cells since Goodrich teaches that riboflavin and light can be used to inactivate microorganisms found in whole blood, blood constituents or separated blood products.

Goodrich teaches that blood components themselves are not damaged by treatment with riboflavin and light, while microorganisms are. As discussed above, there is explicit teaching in Goodrich of what constitutes "microorganisms". White blood cells are not included in that definition. If, as the Examiner argues, one skilled in the art would assume white blood cells could be inactivated because they are part of "whole blood, blood constituents or separated blood products", one skilled in the art must also assume that using riboflavin and light to inactivate white blood cells would not damage the white blood cells, since, according to the Examiner, white blood cells are part of whole blood, blood constituents or separated blood products. This is clearly incorrect.

The Examiner therefore cites the Joshi reference to cure the deficiencies of the Goodrich reference, in particular, for the teaching of the activation of riboflavin by UVB light.

The Joshi reference does teach that riboflavin generates singlet oxygen and superoxide anion radicals upon exposure to UVB light. However, Joshi also teaches that "photo oxidation of dioxyguanosine by riboflavin and UV radiation is of significant importance from the point of view of cell-damaging reactions by activated oxygen species produced by the synergistic action of sunlight and chemical agents. It is now known that activated oxygen species are responsible for skin photosensitization, tumor promotion and carcinogenic properties."

Combining the teachings of Goodrich with the teachings of Joshi, one skilled in the art would think that irradiating blood products with riboflavin and UVB light would produce activated oxygen species which would cause damage to the red blood cells, platelets and plasma being irradiated, and cause tumor promotion and cancer in the irradiated cells. Furthermore, as neither Goodrich nor Joshi alone teach the irradiation of white blood cells with UVB light, one skilled in the art would not think to do this using the combined teachings of Goodrich and Joshi.

The Examiner argues that one of ordinary skill in the art would have been motivated to use the methods taught by Goodrich and Joshi in order to inactivate white blood cells and bacteria, viruses and parasites, and that there is clear motivation for combining the references. As set forth in MPEP 214301(IV), a statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references." *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). Rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR 550 US at ___, 82 USPQ2d at 1398 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

The Examiner has not provided an objective reason to combine the teachings of the references. The mere statement that one skilled in the art would have been motivated to combine the references is not enough to establish a prima facie case.

The Examiner argues that "it would have been obvious to a skilled artisan to characterize the dose-response relationship for the inactivation of white blood cells in order to determine the minimum dose of UVB required for inactivating riboflavin which results in the inactivation of white blood cells" and points to Examples 5 and 6 for support of his position.

However, Example 5 studies the extent to which UV light without riboflavin can penetrate a red blood cell sample. Measuring the depth of UV light penetration into red blood cells is not "characterization of the dose-response relationship for irradiating cells with UV light in the presence of riboflavin" as stated by the Examiner. Firstly, Example 5 does not measure the effect of riboflavin and UV light, as there is no riboflavin present. Secondly, Example 5 does not measure the damage to red blood cells caused by riboflavin and UV light. The definition of penetration is "to pierce or pass into or through" (Random House Webster's Unabridged

Dictionary). Example 5 measures the distance into a red blood cell sample UV light can pass into. This is not measuring the effect of riboflavin and UV light on cell damage.

Example 6 does indirectly study the effect of riboflavin and UV light on platelets by measuring in vitro measurements of platelet function. However, platelets are not white blood cells. Platelets do not have nucleic acids and therefore the nucleic acids can't be damaged by riboflavin and light. Combining the teachings of Ex. 5 and 6 would teach one skilled in the art to measure the distance UV light is able to penetrate into a sample containing red blood cells or platelets. It would not teach them to inactivate the nucleic acids of white blood cells.

In his response to Applicants arguments in the final Office Action, the Examiner cites a secondary reference Meunier to support his position that "it would have been obvious for a skilled artisan to characterize the dose-response relationship for the inactivation of white blood cells in order to determine the minimum dose of UVB required for activating riboflavin which results in the inactivation of white blood cells." See page 6, line 11 of the final office action.

The Meunier reference was never discussed during ongoing prosecution of this application. However, to address the Examiner's arguments completely, Applicants will discuss this newly cited reference.

Meunier describes some consequences of UV irradiation on cells and discusses a variety of assays that can be used to screen for damage resulting from the activation of drugs by UV light. Meunier teaches on page 5 that endogenous photosensitizers such as riboflavin produce reactive oxygen species (ROS) which causes strand breaks in nucleic acids when exposed to UVA light. Meunier goes on to state that "[t]hese DNA damages, albeit certainly efficiently repaired, could be a source of genetic instability."

From these teachings, one skilled in the art would think that the damage to DNA caused by using riboflavin and light would self-repair, and thus would not be a good solution for permanently damaging DNA of white blood cells. This teaches away from Applicants claimed

invention which is directed to substantially maintaining the damage to nucleic acids of white blood cells caused by riboflavin and light.

As taught on page 3, line 18 of Applicants specification, it is toward the method of pathogen reducing blood and blood components by inducing permanent damage to the nucleic acids of pathogens that the present invention is directed. Permanent damage means that the inactivated pathogens are unable to re-activate upon storage or upon infusion into a patient. Meunier clearly does not teach this.

Conclusion

For at least the reasons given above, the Board of Patent Appeals and Interferences should reverse the claim rejections under 35 USC 103(a) and permit allowance of claims 12-15, 17-19 and 22.

It is believed there is a fee of $540.00 due for the filing of a brief in support of an appeal. Please charge this fee and/or any other necessary fees to our Deposit Account 03-2316.

Respectfully submitted,

11-17-2010
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VIII. CLAIMS APPENDIX

Appealed claims:

1 – 11 (Cancelled)

12. (Previously presented) The process of claim 15 wherein the fluid further comprises red blood cells.

13. (Previously presented) The process of claim 15 wherein the fluid further comprises platelets.

14. (Previously presented) The process of claim 15 wherein the fluid further comprises plasma.

15. (Previously presented) A process for inactivating white blood cells which may be contained in a fluid comprising:

adding to the fluid containing white blood cells an effective amount of riboflavin acting as a photosensitizer;

exposing the fluid and riboflavin acting as a photosensitizer to light of an appropriate wavelength to activate the riboflavin acting as a photosensitizer and cause damage to the nucleic acid of the white blood cells

wherein the light to expose the fluid and riboflavin acting as a photosensitizer is in the UVB range; and

substantially maintaining the damage to the nucleic acids of the white blood cells.

16 (Cancelled)

17. (Previously presented) A fluid suitable for transfusing into a patient comprising red blood cells treated by the process of claim 15.

18. (Previously presented) A fluid suitable for transfusing into a patient comprising platelets treated by the process of claim 15.

19. (Previously presented) A fluid suitable for transfusing into a patient comprising plasma treated by the process of claim 15.

20-21 (Cancelled)

22. (Previously presented) A process for providing pathogen-reduced blood or blood components comprising:

damaging the nucleic acid of any pathogenic white blood cells, bacteria or viruses which may be present with the blood or blood components by

adding riboflavin acting as a photosensitizer to the blood or blood components; and

exposing the blood or blood components and riboflavin acting as a photosensitizer to UV or visible light to activate the riboflavin acting as a photosensitizer to fragment the nucleic acid of the pathogenic white blood cells, bacteria or viruses;

wherein the step of exposing the blood or blood components and riboflavin acting as a photosensitizer to light further comprises exposing the blood or blood components and riboflavin acting as a photosensitizer to light in the UVB range.

23. (Cancelled)

IX. Evidence Appendix

None

X. Related Proceedings Appendix

None